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RADIUM

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VOL. XI AUGUST, 1918 No. 5

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

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RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D. with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. XI AUGUST, 1918 No. 5

SOME FACTORS INFLUENCING RESULTS OF RADIUM THERAPY*

JAMES EWING, M. D. (New York).

As the reports of the results obtained in the treatment of cancer by radium multiply from many sources, and as the experience of the users of radium widens, it becomes apparent that this form of therapeutics is gradually becoming established on a basis which will guarantee its permanency and its substantial progress. It is also apparent, contrary to the original impression of many, that the successful application of radium in cancer is a very complex problem, and one that will require years of close study before the real capacity of this agent to deal with many forms of cancer will be determined. I believe it is highly important for the interests of radium therapy that the users of radium, the medical profession, and the public should recognize, that while the methods are standardized in many respects, there are numerous questions that await answer before one can claim radium therapy is entirely beyond the experimental stage. One of the most prominent of these questions concerns the relation of the structure of tumor tissue to the reaction of radium.

My own experience from clinical observation, studies of tumor tissue treated by radium, and examinations at autopsies, leads me to conclude that this is the most important problem before us.

The earliest observations showed that some tumors were highly resistant, while others were remarkably susceptible to radium, and experience shows that those that respond most readily to the simplest test of therapeutic efficiency and diminution in size, are usually cellular and rapidly growing tumors. Conspicuous examples of this class are found

*Read at the Third Annual Session of the American Radium Society, Chicago, June 10th, 1918. In the absence of Dr. Ewing, his paper was read by Dr. W. H. Cameron.

in the lymphosarcomas, and embryonal or anaplastic carcinomas, as teratoid carcinoma of the testis or ovary. These tumors melt away rapidly under radium, and while they may seldom be completely cured by this treatment, the ultimate failure is not due to the inefficiency of radium, but to the wide dissemination of the disease. I have observed several failures of abdominal metastases of teratoid carcinoma of testis to yield to radium, and in each instance autopsy disclosed that the structure of the tumor had become markedly fibrous, and that the tumor had existed for many months. In the same way early and rapidly growing local metastases of mammary carcinoma may often yield readily to radium, whereas older tumors which have become fibrous may show very little or no reduction in size after persistent radiation. Very striking differences are often observed in the reaction of recent as compared with old tumors of Hodgkin's granuloma malignum, and this difference accords with the natural change of structure, the older tumors becoming fibrous.

Thus it becomes evident that in establishing standards of therapeutic results in the radium treatment of tumors, it is necessary to recognize what stage of the growth one has to deal with and not to regard all tumors bearing the same name as identical problems.

There is a considerable number of tumors commonly regarded as refractory to radium, but which respond satisfactorily if one will take sufficient time for the treatment. Chondroma is a slowly growing tumor composed of a moderate proportion of cells and much firm cartilagenous chondrinous matrix which is not susceptiole to ready absorption. Yet thorough radiation by heavily filtered radium will cause many of these growths to stop growing, and after a period of weeks or months there follows a slow absorption. Too powerful treatment may, on the other hand, cause the tumor to break down and become cystic, and these cysts may become infected.

The reports of the results of treatment of osteogenic sarcoma by radium or x-ray, while favorable in some instances, are not on the whole satisfactory. I am inclined to think that this situation is partly due to misconception as to what one may reasonably expect to accomplish in a given time with this disease. From the anatomical standpoint there are three types of this disease. First, fibrous or cellular periosteal tumors. Second, very vascular or telangiectatic tumors, and third, sclerosing osteogenic sarcoma producing dense bone.

In addition, we have tumors of bone marrow cells, myeloma, and also the disease best known as benign central giant cell sarcoma of epulis type. All of these tumors react differently to radium.

Periosteal osteogenic sarcoma can often be controlled by radium or x-ray, but it will seldom show a marked reduction in size in a short period. The reason is that they are often fibrous and tend to produce bone, and if radium slows down the rate of cell growth the tendency to produce bone will be increased, and bone or osteoid tissue is not readily absorbed. One must usually plan to spend a long time in the treatment of such a tumor. I have observed one recurrent case over a period of a year, which remained absolutely stationary for six months, after an initial period of increase, and then slowly disappeared, leaving an apparently normal limb.

Telangiectatic osteogenic sarcoma is a very malignant disease, and when the tumor and destruction of tissue are extensive there is little hope of a successful result by any method. Time is of great but not of prime importance. I believe that this group of tumors should be sub-

mitted to thorough trial by radium and x-ray, and think there is good reason to believe, from a study of many dissected speciments, that at least the earlier stages of such growths may be successfully arrested by radium.

In sclerosing osteogenic sarcoma the process is slow and much dense bone is laid down throughout the marrow cavity and distending and obliterating the periosteum. If the growth of such a tumor were completely arrested, there would be no diminution in size for many months and even then an ebonization of the new bone. I have observed such a transformation of sclerosing sarcoma of the femur covering a period of three years. The growth of bone was completely arrested, but the patient developed epithelioma in the resulting x-ray burn.

Myeloma is usually multiple or systemic, and while the single tumors readily respond to radium, the disease usually progresses with the development of new tumors in other situations. Nevertheless at the Memorial Hospital, we have under treatment by x-ray a diffuse lymphocytic myeloma of the entire shaft of humerus which has steadily receded, a new shaft appearing, and the patient is free from extensions, and is able to work.

Benign central giant cell sarcoma is commonly treated by conservative excision and curettage, but not always successfully. Since this tumor tissue is very susceptible to radium, it would appear reasonable to subject these tumors to radium treatment without excision and even without incision for diagnosis.

The fascial myxosarcomas are often confused with osteogenic disease but they are wholly different in origin and nature. Most of them are myxomatous, not very cellular, but quite vascular, and they contain small or large spindle cells. The large spindle cell variety grows rapidly and early produces metastases, chiefly through the deep or subcutaneous veins. Hence the results of operation are very poor. Their control by radium is not an easy task, and has to be managed with patience and care. After treatment by radium, they may swell considerably and appear to grow more rapidly, but this swelling is due to edema and inhibition of fluids. The tumor tissue itself is easily influenced in all but the large spindle cell variety, and I have seen two of these tumors slowly shrink and disappear after radium treatment, the patient remaining free from recurrence for some months and up to date.

Neurogenic fibroma or sarcoma occurs as multiple tumors of the skin, or multiple tumors of a large nerve trunk, or as solitary large tumors of one or more deep nerve trunks. They are hard and fibrous, or cellular and myxomatous, or more cellular and sarcomatous. They recur persistently after operation, either in situ or by the development of new tumors at other points in the nerve trunk, but they seldom produce metastases. There are indications that radium may be of much service in the treatment of these tumors, either with or without operation. One must not, however, expect that solid fibrous tumors of this type will rapidly reduce in size, but must rather look forward to slow regression requiring a period of weeks or months. An initial period of swelling from edema must also usually be anticipated and the patient and others warned against its misinterpretation.

In the case of osteogenic, fascial, and neurogenic sarcoma, a warning may well be raised against incision for diagnosis. Such incisions may lead promptly to infection, these tumor tissues being extremely susceptible to bacterial growth, and when infection becomes established, the

tissue cannot be treated properly with any method, and progressive sepsis and cachexia develop. I have seen several cases lost in this manner.

The difference in the reaction to radium of squamous cell carcinoma and basal cell carcinoma of the skin has been universally conceded, but not all workers with radium have recognized that similar distinctions exist in the case of several other tumors and especially among tumors of mucous membranes. Certain epidermoid carcinomas of the cervix uteri are composed of small cells consisting chiefly of nuclei, with scanty cytoplasm, and growing in plexiform cords. They are of relatively slow growth and do not early involve the lymph nodes. Ribbert regards these tumors as the analoque of basal cell carcinoma. Other cervical carcinomas tend to develop squamous cells, with pearls and hornification, and they infiltrate more rapidly, and are more resistant to radium. I am not entirely convinced from my own observations that the uterine tumors furnish exact duplicates of the cutaneous growths, but there is considerable variation to their reaction to radium, and it seems desirable that the distinctions mentioned by Ribbert and clearly demonstrable in any series of uterine cervical carcinomas should be kept in mind in the treatment of these diseases by radium. I have several times observed that papillary tumors of the cervix, even when bulky and apparently advanced, have given unexpectedly good results from radium.

The separation of basal cell and squamous cell carcinoma of the vagina is also desirable from the standpoint of radium therapy.

Many of the mixed tumors of the parotid were early found to yield very favorable results with radium. Although these are tumors of parenchymatous glands, many have pointed out their identity, in structure and clinical course, with the basal cell carcinomas, and this fact may explain their response to radium.

In many cases of epidermoid carcinoma the disease is complicated by streptococcus infection of the tumor tissue, and this infection is very prone to extend wherever the tumor cells ramify in tissues or lymph nodes, and the symptoms of bacterial intoxication may dominate the clinical picture. In such cases the reaction to radium, even in palliative doses, is usually not favorable, because the radium inflammation renders the tissues edematous and seems to aggravate the infection. In fact it may be stated that the bacterial sterility of tumor tissue is a matter of first importance in radium therapy, and the presence of bacterial infection accounts for many radium failures, and often forms a contraindication to its use.

Likewise, an unfavorable outcome of several cases of epidermoid carcinoma in accessible situations, I have found to have occurred in patients who were suffering from tuberculosis or advanced syphilis, in the neighborhood of the tumor, or in the internal organs. It has appeared that these complicating general diseases rendered the patients anemic or cachectic, and unfavorable subjects for radium or any other form of therapy.

These observations support the conclusions drawn from the histological study of the reaction to radium, which show that the cure of a carcinomatous process is not wholly due to the destructive effects of radium upon the tumor cells, but depends very largely upon the capacity of the tissues to react with an exudate of leucocytes and with healthy granulation tissue.

Thus the study of radium results, from the laboratory standpoint, emphasizes the importance of at least three factors as determining the

results of treatment: (1) The structural type of the tumor; (2) the complicating inflammatory and nutritive conditions of the tumor tissue, and the soil in which it is growing; and (3) the general condition of the patient. All of these factors influence the therapeutic result quite apart from dosage, filtration, and accurate application of the agent.

DISCUSSION

DR. HENRY SCHMITZ, Chicago—I think the conclusions in Dr. Ewing's paper strike the keynote of radium rays in pathologic therapy. The size of the tumor, the inflammatory condition in which the tumor may be found and the general condition of the patient. From my observation and study there is no doubt that the radium rays will favorably influence some tumors, and some they will not. This is due to the state of the resistance of the patient. All those who have had experience with radium therapy will agree with me that there is a class of patients who will respond very readily to radium therapy, but the general condition will be unfavorable. This means that the general condition is absolutely below par. The question is, has it become below par because of the tumor growth which produces the unfavorable condition in the patient. The question arises whether these tumor cells change in each and every instance, and if they do not change can we still speak of the absolute stopping of the growth? In most instances it seems to me that we can. In other conditions we cause a difference in the condition of the growth so it is changed from a malignant to a benign affair, but it persists.

Another question is whether the tumor has anything to do with it. In many cases the patient suffers severely and becomes greatly emaciated, and it seems to me this condition is caused by absorption of the toxins from the tumor cells. In these cases would it not be a good plan to use mixed therapy? Would it not be advisable to go ahead and remove the degenerated mass of tumor tissue and in this way give the patient a better chance of recovery? In some of my recent work I have gone ahead and subjected the patient to radical removal of the breast or uterus and then used radium and in the few cases in which I have done this the results have been most promising. The patients have made a slow recovery and are in much better condition than before. Of course it is impossible to say whether they will remain so or not.

I wish to impress upon the members of this Society the change produced in transforming pathological into benign tissue. It is really astonishing how much can be accomplished in this way. It seems to me that it is impossible for anyone to establish a fixed law which you can apply to the same type of tumor in every case. Some tumors will disappear and it will not matter what the structure is, and some will not. Why some cases of basal cell carcinoma and some of squamous cell will not do so well I cannot say, but it seems to me that the patient has a much better resistance in some cases. In some instances of squamous cell carcinoma the patient does not do well at all, may become decidedly worse, and the growth of the tumor is stimulated. We see that all the time and no pathologic explanation can be found for it. There is no doubt that on an average we can apply these observations, but the whole thing does not work under the same rule at all times. The size of the pathological condition is of great value and we should base our technique upon this observation.

There is another question which we have not settled satisfactorily, and that is the proper dosage and the proper manner of the application of radium to these growths. In some cases we obtain results with very

minute doses and in some with excessive doses. In one case of carcinoma I used 100 mgs. of radium element for a few hours and the dose caused no destruction of cells. I did this for six weeks and the patient became worse. I then left the radium carrier on for thirty-six hours and the tumor disappeared. If I had used the small, interrupted dosage which has been highly recommended to me, the tumor would have kept on growing, but I changed my mind after treating the man for six weeks without result, applied a very large amount of radium and the tumor disappeared. So we often find conditions where we may apply a very small amount and get excellent results, where in another case we get no reaction at all. I am sure the pathology had nothing at all to do with that, and if we could find some way in which our pathological observations would be brought into accord I think we would advance a great step in our specialty.

Dr. Robert Abbe, New York City—This paper is one of the most important that I have listened to and I think the Society is fortunate in having such a man as Doctor Ewing to give us such a paper. We need a gyroscope to keep us steady and Doctor Ewing is feeling his way out and trying to formulate laws, but he is failing to make laws that stand. He says one thing this year and next year changes his mind, but it is perfectly right that he should. As Doctor Schmitz says, every case differs in its resistance and the type of pathological tumor is less important for us to know about than the results we are getting in certain types of cases. I do not believe we can say that a certain type of tumor will always disappear under radiumization. While it is possible that because it is a fibroid it will not yield, it is equally true that the myelomata yields very easily, but it yields also to the x-rays. I will speak only a moment on this subject for there is so much to say that one could talk for hours.

One point I would like to speak upon is the contamination of tumors by infection. As we look at these patients and see the mass of tumor and the putrid odors arise from a large exudate, we say it is hopeless and there is no use, but we put on the radium and pretty soon the discharge lessens and then the odor clears up, the patient feels better, the hemorrhages cease and a little later the anemia clears up, the patient looks better and the uterine cancer which has been so offensive that her friends could not tolerate her and she could hardly tolerate herself almost clears up. I have seen this take place especially in many tongue cancers that have been said to be hopeless. We think we can't waste our time on them, and then the tumor begins to clear up, the odor disappears, and finally there is left only an infiltrated neoplasm on the surface apparently, the necrosis disappears and the patient is perfectly happy over his improved condition. Then you think you have done your patient a great deal of good, the patient has only a remnant of the old fibrous growth in the tongue—and then it lights up again. What you achieved was a bacterial cure—you reduced the bacteria, and the same thing happens in the uterine cancers.

So I would hardly acknowledge to myself what Doctor Ewing has so clearly stated, that these cases are hopeless. I think on the contrary that we can do a great deal of good for the patient, and perhaps can keep up the improvement for a long time.

Dr. W. H. Cameron, Pittsburgh, Pa.—Not being familiar with many things that Dr. Ewing has said, I do not suppose I should attempt to close the discussion. One thing that strikes me very forcibly is that Doctor Ewing, who is a noted pathologist, advises against incision for diagnosis.

Many of us have made an incision for diagnosis and we have seen those cases go from bad to worse shortly after. I am glad that a man of Doctor Ewing's standing advises against such a practice. We will have to let down on laboratory diagnosis of many of our cases and depend on clinical observation.

I want to emphasize what Dr. Ewing and Dr. Abbe have said about the inflammatory conditions. I think this is the most important thing we have before us.

Another thing is resistance. Dr. Gaylord, of Buffalo, has probably worked that problem out better than anyone else. He has shown that anesthetics and bleeding break resistance, and this is probably the reason many of our cases clear up so promptly—we do not break resistance unless we administer a too large dose of rays. When we operate the thing of primary importance should be the control of the bleeding, and the administration of gas instead of ether and chloroform. The thing for us to do is to find methods that will build up our patients, at the same time we are using the radium.

RADIUM TREATMENT OF SCARS*

With Clinical Notes on Military Orthopædic Cases.

By Walter C. Stevenson, M. D. Dub.,

Captain (Temp.), R. A. M. C., Blackrock Military Orthopædic Hospital; Surgeon, Dr. Steevens' Hospital and Orthopædic Hospital, Dublin.

One of the problems of military orthopædic surgery is the treatment of painful and adherent scars, which for the present purpose includes only simple fibrous-tissue formation and adhesions, the result of wounds and inflammation, and not the pathological changes which may supervene, such as keloid and epithelioma.

Troublesome scars can frequently be excised with the best and quickest results, but as frequently it is not desirable to touch them with a knife. Excellent results are obtained by gradual stretching of scars and adhesions by screw splints and elastic apparatus, or in suitable cases by forcible stretching under an anæsthetic, always with advantage combined with some means of more slowly but progressively freeing the part, and increasing its functional use and vascularity, such as curative work and exercises, massage, ionisation, hydrotherapy, and, as I have observed, treatment with radium. Large doses of hard x-rays should act similarly, but personally I find radium more convenient to apply and safer to use on account of the accuracy with which the dose can be estimated, administered, and recorded for future reference. (2).

Radium, or rather the hard beta- and gamma-rays of radium B and radium C—I always use radium emanation as their source—appears to act as a true "fibrolysin." Clinically such radiation alters the consistence of the scar, making it soft and pliable, and apparently enables the surrounding adherent tissues to free themselves from the original tough fibrous mass.

*Reprinted from the Lancet, March 23, 1918, pp. 432-433.

Radium and x-rays are undoubtedly the most potent and physical agents we possess for effecting metabolism of animal tissues. It has some action on every individual cell radiated. The effect, probably due to its ionising properties, is not merely local, as some of the hard rays of radium will not be stopped by several feet of human tissues. In this respect it has a great advantage over electrical ionisation, hydro-therapy, massage, etc., but I am far from suggesting that radium can replace their usefulness.

Two cases were here recorded in which was shown the analgesic effect of radium treatment, an important factor in its usefulness. Morson's (3) experience is similar.

That radium has a most powerful and rapid effect on the tissues and the blood-supply is beyond question. A patient I treated with emanation needles for a fungating growth in the floor of the mouth, involving under-surface of tongue, showed this in a most striking manner, quite obvious to all who saw it. Morson's micro-photographs confirmed the possibility of these rapid and definite changes. (3)

Illustrative Cases

Radium affects normal as well as pathological cells. I have no knowledge of the histological changes it produces in scars. Clinically there appears to be a fairly rapid, but not a marked, œdema of the tissues. A red scar becomes whitish in 3-5 days and about the tenth day after treatment it turns to its former color. During the white stage the scar is painless and the pain returns when the original red color is restored. The anæsthetic effect is further illustrated by Case 4.

*Case 4.—Pensioner in Blackrock Military Orthopædic Hospital. Longitudinal shrapnel wound over dorsum of first inter-phalangeal joint on left middle finger causing some bony displacement and involving extensor tendon. Little or no voluntary movement in joint which was held at angle of 125°. Any forced movements caused severe pain. He could move distal joint freely. I sent him to my house and applied 51.4 mc. (millicuries) of emanation in my applicator for three and a half hours. Immediately on its removal patient was delighted to find he was able to move joint freely, through an angle of 30°, which I verified by measurement on a graft. I could forcibly straighten finger and bring it to right angle at joint without hurting him, at least so he assurred me.

There was no question of mental suggestion in this case: in fact, I did not expect much change for two or three days. The man thought he was wasting his time until he saw the effect of treatment. Personally, I am convinced I could not have obtained such a quick result, but I believe, permanent gain as far as movement goes, by any other method of treatment. But I also recognize that it is only a stage in the treatment, which must be supplemented by the patient's personal efforts in the workshops and general orthopædic treatment.

Besides four of the cases above eight others were treated with radium for scars during last August.

Case 7.—Private B. was treated for painful adherent scar on front of right forearm on August 8th, 1917. Two days later scar was less adherent and less painful. On August 29th, 1917, marked improvement in whole forearm, less pain, and more power in hand, and drag of scar on dorsi-flexion of wrist was scarcely perceptible, though before treatment very well marked.

Case II.—Private M. had extensive scar firmly adherent to, and taking contour of broken right clavicle for about two inches of its center.

*A number of cases are omitted owing to lack of space.

Unable to abduct arm to right-angle, and this movement caused great pain. He was treated on August 9th, 1917, by surface application for 18 hours of two applicators from London Radium Institute, each containing 24 mc. I quote the notes of Miss Despard, (5) masseuse in charge at Blackrock Hospital:—

"No improvement noticed for a day or two; after this there was no pain on movement of shoulder joint, and movements of abduction and extension had improved greatly. The scar had become pale in color and much softer. On 16th patient complained of pain on shoulder above and behind scar when touched and scar had deepened in color, but movement in shoulder-joint, especially abduction, had improved. On August 29th, 1917, great improvement all round. Scar looser. Movements freer and stronger."

My note on the 28th states: "Scar very much freer and cicatricial area now nearly level with surrounding skin, and not depressed and markedly attached to collar bone as previously. Movements of arm much freer also and voluntary control of shoulder muscles distinctly increased in strength, improving power and usefulness of arm as a whole. He can abduct arm well above a right-angle. The marked action of the radium in this case would appear to be due to the removal of the inhibiting effect of the painful scar on the patient's voluntary movement."

Major W. S. Haughton, R. A. M. C., subsequently removed the scar, as it interfered with wearing of patient's equipment. Major Haughton tells me he was struck at the operation by the ease with which he was able to remove the scar and bring the skin edges together.

CASE 12.—Treatment with radium of scar on dorsum of foot of Private S. near big toe resulted in freeing scar from tendon and bone, with improvement in functional varus position of foot, and enabled him to touch ground with big toe.

Dosage—Result of Treatment

Two cases showed that the question of dosage is of importance, as too large a dose may do more harm than good, while with a small dose the maximum benefit cannot, I believe, be obtained.

The dose I give is a large one, and ranges from three-quarters to seven-eights of that which I know from experience of my apparatus in malignant cases will cause epilation, erythema, and sometimes blistering or slight ulceration of the skin. With the standards I employ the erythema dose is from 400 to 420 mc. h. (millicurie-hours). The applicator is a shallow box, its lower surface 2 by 3 cm. in area, the whole box and lid being made of lead 1.57 mm. thick. Before it is applied the whole box is covered with two layers of lint, or a slightly greater thickness of wool and a couple of layers of adhesive plaster, to cut off the soft secondary rays from the lead. This makes a package which covers and radiates about 3 by 4 cm. of the patient's skin, against which it is fixed by strapping and a bandage.

The radium emanation is supplied to me by the Royal Dublin Society Radium Institute in fine glass capillaries about 1.75 cm. long described elsewhere, (4 7) I distributed at least eight capillaries, evenly and parallel to one another along the bottom of the box, and fixed them in position by paraffin, thus obtaining, at the distance they are from the skin, a fairly uniform radiation.

The dose I employ per area treated for a thin part like the hand is about 320 mc. h., and for a more fleshy part 360 mc. h. For instance, utilising an average of 40 mc., the time it would be left on the hand is

obtained by dividing 320 by 40—i. e., eight hours, similarly for the arm nine hours.

As the emanation in the applicators kindly lent me by Dr. J. E. A. Lynham from the London Radium Institute is less concentrated—i. e., the applicator is 4 x 4 cm., and is filtered to a greater extent by 2 mm. of lead, 40 mc. (equivalent to 40 x 1.81 mg. of $RaBr_2 . 2H_2O$, their standard of measurement) may safely be applied for 10 hours on the hand and 11½ on the arm.

If x-rays are used for the treatment of scars, I would suggest as a suitable dose a full Sabouraud, or 8X of Kienboeck (an epilation, or 8/10ths of an erythema dose), measured after the rays have passed the filter of at least 1 mm. of aluminium. (8)

Most of the Blackrock cases reported above were patients of Major Haughton, and I am much indebted to him, Lieutenant-Colonel W. I. de C. Wheeler, and Major T. J. Potter, officer in charge, for the facilities they have afforded me in treating their patients and carrying out my investigations. I am also indebted to Miss Despard and the ladies of the Massage Department for their careful notes, as practically all the patients were attending there for treatment.

The improvement with massage and electricity, etc., is often so gradual that many patients profess to think that it is doing them no good, and they often become depressed. Any treatment, therefore, which gets them over the dead point or apparently stationary stage in the progress of improvement, as I believe radium treatment can in suitable cases, is of great benefit, not only on account of the actual improvement obtained, (7) but also because of its mental effect. I asked Miss Despard to give me a general statement as to the usefulness or otherwise of radium treatment from the point of the masseuse. Her report, dated August 30th, 1917, which, I think, states the facts very fairly, is as follows:—

"In every case, except one, of the patients under my care, who have been treated with radium, I have noticed an improvement in the mobility of the joints affected. The scars seem to become paler in color, much softer and less adherent to the underlying structures; and massage treatment and exercises have been continued with much better results after an application of radium than before it. The patients complain of less pain in the scar on movement, and in some of the cases treated the improvement in mobility has been very marked."

Recent Unhealed Wounds

The patients I treated in Blackrock, including 16 more recent cases, mostly hands, where similar effects were observed, were suffering from the effects of old healed wounds received in 1915 and 1916, and had been given months of massage and similar treatments in general hospitals and command depots. During 1916 I used radium on some of my military patients in Dr. Steevens' Hospital for recent unhealed gunshot wounds. The results, I think, are worth recording, as they at least prove that small doses of radiation do no harm, and probably hasten the healing process and restoration of function.

Case B.—Lieut. M. had painful sinus 5½ inches long extending from perineum to right femoral vessels for over two months. On June 27th, 1916, I inserted silver tube containing 9 mc. of emanation and radiated bottom of sinus, halfway down and near its external opening, leaving tube three hours in each place. I then re-inserted the drain. Next day increased amount of pus, but no pain. On July 4th no pus to be seen; I could not get in smallest rubber drain. From that date sinus healed.

Case E.—On December 12th, 1916, I inserted tube containing 4.4 mc. of emanation into sinus of bullet wound in front of Private A.'s right elbow for 10 hours—44 mc. h. My note four days later says: "Patient states as result of treatment more pus, but arm freed from soreness, and can flex it much better, and pronate and supinate it much easier."

Case F.—On December 13th, 1916, silver tube containing 3.6 mc. of emanation was left in two positions for six hours each in sinus of Private S., extending from outer side of left thigh to neighborhood of sciatic nerve (total 43.4 mc. h.). Three days later patient stated that treatment had made him much freer and that he had much more feeling in his leg.

I can vouch for the fact that these two men (Cases E and F), who were in different wards, were genuinely pleased with the results of treatment. The power of extension in the elbow and movement in the radio-ulnar joint were markedly increased in Case E, while the other patient used his limbs more freely and walked with greater confidence. Whether these results were due to an analgesic effect on the nerves, or some freeing of adhesions, or were simply psychological is a matter of conjecture, but, personally, I cannot attribute them to the last cause alone. I may mention that, in order not to vitiate the value of my observations, I never suggest to the patient what the effect of treatment may be, so as to eliminate the purely psychological. It is obvious that the effects of any treatment on subjective symptoms in such cases can be masked or exaggerated according to the temperament of the patient and the pessimism or optimism of the observer, however fair the latter may try to be. I have, therefore, entered rather fully into the question of dosage, so as to enable other workers to confirm or refute the value of this line of treatment.

Conclusions

1. Radium has a distinct sphere of usefulness in the treatment of scar tissue and fibrous adhesions.
2. It is a valuable adjunct to other methods of orthopædic treatment, especially by shortening their duration.
3. Its effect is rapid, sometimes immediate.
4. It softens and mobilises scar tissue.
5. It appears to facilitate subsequent removal of the scar by the knife.
6. It enables structures, like tendons adherent to the scar, to free themselves.
7. By loosening tendons and stiff joints it improves the functional power of the part.
8. It possesses the advantage of acting, to some extent, as an innocuous local anæsthetic for about a week.
9. It is particularly useful in treating scars and adhesions in the hands and fingers.
10. It is easily applied to the surface of the skin, and by this method causes no inconvenience to the patient.
11. To obtain the best results a single large dose is necessary.
12. The dose should not be so great as to produce inflammation of the skin.
13. With suitable dosage it appears to produce no ill effects.
14. In small doses it appears to hasten the healing of wounds, and to allay the painful inhibitory effects of the products of inflammation.

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Dublin, September, 1917.

REPORT OF THE CHEMICO-PHYSICAL LABORATORY* THE RADIUM INSTITUTE, LONDON.

BY

W. L. S. ALTON, F. I. C., *Director.*

The output of applicators from the laboratory has been well maintained during the past year, and notwithstanding the diminution of personnel engaged on this work, opportunity has been taken to carry out some investigations of interest in radium therapy.

EMANATION APPLICATORS.

A table is given for the numbers made in 1916 and 1917.

	1916	1917.
No. of Emanation tubes and applicators prepared....	593	587
Initial activity in terms of Radium Bromide .....42.42 grammes		53.48 grammes

Eliminating one tube of the high activity of 250 mgr., and 52 capillary tubes (averaging 20 mgr. each) for the very small platinum needles described in last year's report, the average strength of the tubes and applicators was approximately equal in activity to 98 mgrs. It is noticeable that though rather fewer applicators were made in 1916, the total activity was more than 26 per cent. higher; this increase in efficiency was due to a rigid economy in the use of returned apparatus, the emanation therein contained being either used for the preparation of radio-active water, or for the preparation of new applicators as the occasion arose.

Five applicators were sent to Scotland, and eighteen to Ireland, mostly for work in a military hospital.

*Reprinted from the Report of the Radium Institute, London, from January 1st, 1917 to December 31st, 1917

Inasmuch as in any applicator charged with emanation, the rays are derived from the active deposit maintained on its internal walls, it is obvious that by varying the contour of the containing vessel, the intensity of the radiation will be considerably modified in its distribution. Two types of applicators have been tried, one a hemisphere, the other a blunt cone, and both appear to be useful in certain cases where it is desirable that the marginal radiation should be greater than the central radiation. These containers are blown from glass tubing, and are sufficiently thin to allow most of the radiation to be used; the sides of the containers are screened with 1 millimetre of lead, the bases being unscreened. Further experiments are being undertaken with a view to extending the usefulness of this type of applicator.

RADIO-ACTIVE WATER.

	1916.	1917.
No. of Bottles of Radium Emanation Solution distributed	10836	7163
Total output in litres	3030	1790

The initial strength of the solution has been maintained at between 1.5 and 2.0 millicuries of emanation per litre, as experience has shown that this strength is the most suitable for use.

RADIUM APPLICATORS AND MEASUREMENTS.

	1916.	1917.
No. of Radium applicators prepared	6	4
No. of measurements of radio-activity	4	5

In addition, most of the applicators in use at the Institute have been remade or repaired during 1917, and the conclusion has been reached that it was necessary to obtain a more permanent method of fixing radium salts to flat applicators than the one which has hitherto been adopted, *i. e.*, the employment of amber dissolved in linseed oil. A great number of substances were experimented with, and two were chosen as being likely to prove suitable; one is a condensation product of phenol and formalin known as oxy-benzylmethyleneglycol-anhydride, the other is a dental vulcanite absolutely free from mineral matter.

Both materials resist water, most solvents, antiseptics, and acids, they can be heated to 144°C. with safety: they take a high polish, and can be applied in thin coats.

They neither of them resist the action of alkalies, but this exception is not of great importance. Of greater importance is the ease with which an applicator made from either of these materials can be broken up, and the radium sulphate extracted, should occasion arise, as both substances go into complete solution in hot concentrated nitric acid, leaving the radium sulphate easily recoverable. The resistance of these new materials to the action of radium can only be determined after a prolonged period, and it is hoped that it will be possible to report upon them favourably as the result of a year's experience. Up to the present, there has been a total absence of the cracking and blistering which occurs in* "full strength," applicators coated with the best resin and oil varnish, sometimes after six months' use, which has necessitated frequent revarnishing and the temporary withdrawal of the applicators from use.

Further, grants of emanation have been made from time to time for the use at lectures, and for the prosecution of researches into problems connected with the war.

*10 milligrammes of radium bromide per sq. cm. of surface.

REVIEWS AND ABSTRACTS.

Sir Ernest Rutherford, F. R. S. (Manchester, Eng).—The Problems of Radioactivity. Abstracted in Brit. Med. Jour., April 13, 1918.

"In the first Silvanus Thompson Memorial Lecture, delivered before the Rontgen Society on April 9th, Sir Ernest Rutherford, F. R. S., reviewed the various lines of scientific investigation opened up as a result of the discovery of x-rays. In a tribute to the first President of the Society, in whose honor the lectureship was instituted, he mentioned that on the morning that the late Silvanus Thompson read of Rontgen's discovery he set to work, and by nightfall had succeeded in producing what was probably the first x-ray photograph taken in this country. The outbreak of war, Professor Rutherford said, had caused an almost complete stoppage in the great tide of advance in pure science, but the lull afforded a suitable opportunity for looking back with some degree of perspective over the ground covered during the last twenty years. Undoubtedly the discovery of this new type of radiation marked the beginning of an epoch in physical science and had brought about a revolution in ideas of the nature of matter and electricity almost as marked as that produced in biology by the theory of evolution. The two decades from 1895 to 1915 had been a period of pioneer advance over a new and fertile territory, with the almost daily discovery of interesting facts and the gradual unfolding of fundamental ideas. The directions of advance which had been stimulated by the discovery of x-rays included investigation on the ionization of gases, electrons, the diffraction of x-rays by crystals, and, most important of all, the phenomena of radioactivity, which was an even more direct consequence of the discovery of x-rays than the work on the electron. The sequence of changes in uranium, radium, thorium, and actinium had now been followed out, not indeed completely, but in the main part. No doubt there would still be in the future considerable developments as the result of investigations of the multiple transformations of the atom, but as a whole, apart from a few outstanding difficulties, like the origin of actinium, the transformation of radioactive bodies was fairly well understood. A fundamental discovery, which had been completely verified just before the investigation was broken off by the war, was that certain radioactive elements were inseparable from one another —mesothorium and radium, for example—and this opened up a conception which must of necessity exercise a profound influence on all work on atomic weights, and lead to a close examination as to whether any of the ordinary elements were a mixture of "isotopes." Professor Rutherford went on to refer to the titanic violence of the explosion in the radioactive atom, shown by the expulsion of α particles at great speed and the ejection of electrons with nearly the velocity of light, accompanied by intense x-rays of much greater penetrating power than any that could be excited by an x-ray tube. He believed that there was very little hope at present of obtaining tubes which could compete with radium or thorium in providing a source of x-rays of very short wave length (and accordingly of great penetrating power). The gamma rays of radioactive substances had proved to be of much shorter wave length than was previously supposed."

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W. S. LAZARUS-BARLOW, M. D. (London). Attempt to Produce Carcinoma by Radium. Proc. Roy. Soc. Med. 1918, XI, Sect. Path. 1. Abstracted in Brit. Med. Jour., Dec. 15, 1917, p. 794-5.

Lazarus-Barlow described an attempt at the experimental production of carcinoma by means of radium. He showed microscope slides and a considerable number of lantern slides from rats and rabbits in which he had endeavored to produce carcinoma experimentally. In the case of the rat minute tubes containing radium in amounts of the orders one hundred-millionth to one tenth mg. (calculated as element) were introduced beneath the skin.

"The quantities of radium element in the entire series of tubes increased in geometrical progression (the factor being 2) from 3×10^{-8} to 3×10^{-4} mg. Owing to the absence of recognizable histological changes with these small quantities, tubes were prepared with amounts of radium increasing to a maximum of 0.15 mg. of radium calculated as element."

These experiments were undertaken on the basis of the facts that exposure to x-rays caused squamous cell carcinoma of the hand, and that small quantities of radium had been demonstrated by him to be of frequent occurrence in carcinomatous tissue. In the case of the rabbit small gall stones obtained from the human subject and proved to be devoid of radium by alpha ray electroscopic analysis were artificially impregnated with radium and introduced into the gall bladders of the animals. These experiments were based on the the fact that he had found a marked difference between the radium content of gall stones in man according as they were associated with cancer of the gall bladder or not, gall stones associated with cancer of the gall bladder containing relatively large quantities of radium, whereas gall stones associated with cancer of other parts, or unassociated with cancer, contained mere traces of radium or none could be detected. The experiments were commenced in 1912 and were not yet complete. He had not succeeded in producing in the animals the clinical condition known in man as cancer, but in the skin of rats he was able to produce, by means of suitable doses, an irregular, considerable overgrowth of squamous epithelium which sent processes into the corium, was frequently supplied with well-marked cell nests, and was indistinguishable histologically from a very early squamous cell carcinoma in man. This condition could be produced at will, but if the action of the radium persisted the newly formed cells came under its destructive influence, and if the radium were removed the skin condition receded with some rapidity, leaving merely a thin scar tissue devoid of hair and hair follicles. The gall bladder of rabbit experiments showed a more advanced condition, and a marked contrast obtained between the appearances of the gall bladders according as the gall stones introduced experimentally into them contained radium or not. Whether containing radium or not there was a great thickening of the connective tissue of the gall bladder, and this Dr. Lazarus-Barlow ascribed to the mere presence of the gall stones as a foreign body. But a fundamental difference obtained in the behavior of the columnar epithelium lining the gall bladder according as the calculus which it contained was radium-free or impregnated with radium. If the calculus were radium-free the most that occurred was a slight polypose overgrowth of the epithelium with an excessive formation of mucus; there was no tendency of the epithelium to invade the wall of the gall bladder. On the other hand, when the lining membrane of the gall bladder had been exposed to the action of a gall stone containing radium the epithelium showed changes indistinguish-

able from those occurring in columnar cell carcinoma in that there was an irregular growth of the epithelium which projected into the cavity of the gall bladder and invaded the thickened wall of the viscus in an irregular manner. As a consequence of the invasion, parts of the thickened gall bladder wall showed the presence of irregular tubules lined with columnar epithelium, grouped in irregular fashion through a less or greater thickness of the gall bladder wall and usually preceded by a zone of lymphocytes. In one rabbit a metastatic focus exactly recalling the appearance of the gall bladder itself was found in a distant part of the liver. This was the sole metastasis found in the entire series of experiments, which involved 122 rats, 6 radium gall stone rabbits, and 3 control rabbits. Reference was made to experiments on the same lines carried out on mice at an early period of the research. In these animals the radium was not contained within tubes, and though introduced beneath the skin in the axillary region in the form of an insoluble sulphate or silicates, was found to disappear from the body within a few weeks. In addition, it was not found possible to keep the animals alive for a prolonged period. Nevertheless, of 67 radium mice living six months after inoculation, 5 developed definite malignant tumors of the mamma (one animal bearing two primary tumors) and 7 other animals developed doubtful tumors (one papilloma and 6 nodular masses, chiefly in the neck, as large as peas, oscillating in size and finally disappearing). Thirteen control animals inoculated in the same way, but without radium and also living six months after inoculation, showed no tumor formation whatever.

Professor S. G. Shattock, whilst fully recognizing the value of the results, and the prospect they opened up of further developments in experimentation upon the etiology of carcinoma, did not consider that the lesions could safely be regarded as more than precancerous. The downgrowth of the epidermis in the rat's skin in no case transgressed the limits of the corium; and on the removal of the radium the changes, instead of progressing, disappeared. In regard to the proliferative changes set up in the mucosa of the gall bladder by the action of radium introduced into gall stones, those seen in the bile ducts in coccidiosis of the rabbit's liver were quite as pronounced. The speaker held that for the production of carcinoma there still remained a second factor which needed discovery. The author's view that this consisted in a lessened resistance required scientific demonstration; nor was it logically the only other possibility, for there might be a second *extraneous* factor, such as the access of an ultramicroscopic virus. A further point against the change in the gall bladder being carcinomatous was the circumstance (as the author stated in answer) that the epithelial cells did not yield the proper Altmann granule test. Amongst the author's results there was one in which a metastasis had occurred in the liver; but here a second extraneous factor might have come into play, and the inflammatory proliferative process have been followed by the growth of a proper carcinoma.

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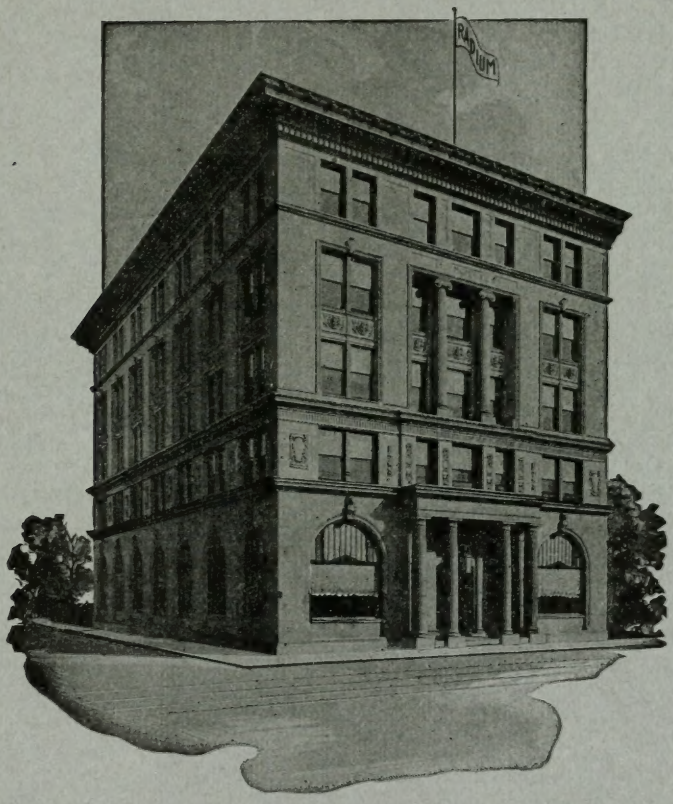

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